April 27, 1948.

Dr. H. B. Newcombe,
National Research Council,
Atomic Energy Project,
Chalk River, Ontario.

Dear Newcombe,

I was very glad to hear from you; I wish we had had time for a more detailed discussion at Chicago.

The conclusioms which you appear to have adopted from your mutation experiments are very close to my own. I may have told you that it "looked as if" the sectored colonies were rather smaller than the non-mutants, suggesting an increased lag in mutants. The plateau and decline in the UV response curve also shows that the mutated cells are rather more sensitive than the others. But why do you think that reduplication is unlikely? The two and four nuclei per coli cell are plainly seen in Robinow's and Boivin's photographs of Feulgen and Giemsa stained material. One hardly needs to go any further. However, the "apparent" lack of mutations in non-dividing cells is particularly well accounted for this way, as is the occurrence, if I recall your work correctly, of a burst of mutations during the early divisions of a new culture.

I am too busy now working with the mutants themselves to have much time to consider the mutation process. The frequencies of induced mutation are sufficiently high (more than 10^{-4} with a dose leaving 10^{-6} survivors) possible I think, to make the method quite feasible. The occurence of recessive lethals must be taken into account in plotting the frequencies of sectored and intact mutants.

Because of its cytological inhomogeneity, the culture of E. coli is not in my judgment very satidfactory material for mutation studies. A priori, I would think that spores of members of the B. subtilis group would be more suitable, since these are apparently uninucleate. On the other hand, the vegetative cells are multinucleate so that one would have an opportunity of correlating genetic behavior with cytological appearance. Many subtilis phages have been described in addition certain related organisms, e.g. B. globigii, B. aterimus, B. niger are deeply pigmented, and would probably throw off albinos which could be used to follow "sectorial" mutations. I started a bit with B. globigii, but the pressure of other work has made me leave it.

From the content of your letter, I gather that you have been able to justify bacteria and bacteriophage. With best regards,

Yours sincerely,

Joshua Lederberg.